A watertight fetal repair reverses hindbrain herniation and improves neuromotor function in spina bifida lamb model

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Objective

Experimental and clinical research have demonstrated that prenatal anatomical two to three-layered repair of myelomeningocele improves neurologic outcome. The reason why less than 50% of clinical patients have complete reversal of hindbrain herniation (HH) and improvement of neuromotor function remains uncertain. One potential reason is incomplete closure, hence potentially leading to persistent leakage of cerebrospinal fluid (CSF). We aimed to determine the efficacy of a watertight fetal repair in the spina bifida (SB) lamb model, using intra-operative testing.

Methods

75-day lambs (term=145d) were randomly assigned to undergo standardized SB induction consisting of >4cm circular skin resection, ≥5-vertebral level laminectomy, durectomy and myelotomy. They were assigned to 3 groups: unrepaired SB (SB group) or standardized 2-layer repair at 100d using watertight Duragen® patch and skin closure. A fluorescein test was done to determine whether the closure was watertight (watertight group) or not (not-watertight group). Lambs were delivered at term (mean=143d). At 1-2d postnatally, primary (HH on Magnetic Resonance Imaging [MRI]) and secondary outcomes (skin closure, CSF leakage, neuromotor function, ventriculomegaly on MRI, Motor/Sensory Evoked Potential (MEP/SEP) measurements) were collected. Statistical analysis compared the repaired to the unrepaired SB fetuses.

Results

Of the 25 fetuses, 69% (6/9 SB), 78% (7/9 watertight) and 43% (3/7 non-watertight) respectively survived. Compared to unrepaired SBs, lambs from both repaired groups had complete skin closure and a low CSF leakage rate (1/7 in watertight, 1/3 in not-watertight vs. 6/6 in SB), yet no reversal of ventriculomegaly. Only watertight repair induced complete reversal of HH (100% vs. 17% in SB; p=0.0014), better neuromotor function (4.0±1.00 vs. 1.1±0.27 in SB; p=0.0001) and presence of hindlimb MEPs (100% vs. 0% in SB; p=0.0286). However, non-watertight repairs had only 67% of HH reversal (p=0.1515), poor neuromotor function (1.1±0.00; p=0.5551) and low presence of hindlimb MEPs (30%; p=0.4286).

Conclusion

In the lamb model, watertight 2-layer fetal SB repair reverses HH and improves neuromotor function. Non-watertight closure does not have the same effect.